

*Amendment and Response Under 37 C.F.R. §1.116 - Expedited Examining Procedure**Page 2 of 8**Serial No.: 09/829,872**Confirmation No.: 7416**Filed: April 10, 2001**For: NUCLEAR MAGNETIC RESONANCE METHODS FOR IDENTIFYING SITES IN PAPILLOMAVIRUS E2 PROTEIN***Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. **(Currently Amended)** A nuclear magnetic resonance method for identifying a ligand-binding site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of chemical shifts for atoms of a mixture comprising a ligand and the HPV-18 strain of papillomavirus E2 protein; wherein the chemical shifts are assigned to atoms of the protein;

providing a second set of chemical shifts as listed in Table 1; wherein the chemical shifts are assigned to atoms of the DNA-binding and dimerization domain of the HPV-18 strain of papillomavirus E2 protein;

comparing the first set of chemical shifts to [[a]]the second set of chemical shifts as listed in Table 1; and

identifying at least a portion of the atoms that exhibit changes in chemical shifts, wherein the site comprises the identified atoms and is a ligand binding site.

2. **(Previously Presented)** The method of claim 1 wherein providing the first set of chemical shifts comprises:

providing a mixture of the ligand and the HPV-18 strain of papillomavirus E2 protein;
allowing the ligand to interact with the HPV-18 strain of papillomavirus E2 protein;
obtaining a nuclear magnetic resonance spectrum of the mixture; and
measuring chemical shifts of atoms from the spectrum.

3. **(Original)** The method of claim 2 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.

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6. (Previously Presented) The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

7. (Original) The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.

8. (Original) The method of claim 1 wherein identifying at least a portion of the atoms comprises identifying at least one nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

9. (Withdrawn-Currently Amended) A nuclear magnetic resonance method for identifying a ligand-binding site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first ¹H-¹⁵N heteronuclear single quantum correlation spectrum of a mixture comprising a ligand and the HPV-18 strain of papillomavirus E2 protein;

providing a second ¹H-¹⁵N heteronuclear single quantum correlation spectrum as illustrated in Figure 2; wherein the spectrum is of the DNA-binding and dimerization domain of the HPV-18 strain of papillomavirus E2 protein;

comparing the first ¹H-¹⁵N heteronuclear single quantum correlation spectrum to [[a]] the second ¹H-¹⁵N heteronuclear single quantum correlation spectrum as illustrated in Figure 2; and

identifying at least a portion of the amino acids having atoms that exhibit changes in chemical shifts, wherein the site comprises the identified amino acids and is a ligand binding site.

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10. (Withdrawn) The method of claim 9 wherein providing the first spectrum comprises: providing a mixture of the ligand and the HPV-18 strain of papillomavirus E2 protein; allowing the ligand to interact with the HPV-18 strain of papillomavirus E2 protein; and obtaining a ¹H-¹⁵N heteronuclear single quantum correlation spectrum of the mixture.

11. (Withdrawn) The method of claim 10 wherein allowing the ligand to interact comprises allowing the ligand and the protein to reach a binding equilibrium.

12-13. (Canceled)

14. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

15. (Withdrawn) The method of claim 9 wherein identifying at least a portion of the amino acids comprises identifying at least one amino acid having a nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

16. (Canceled)

17. (Previously Presented) A computer-assisted method for identifying a ligand binding site in a DNA-binding and dimerization domain of an HPV-18 strain of papillomavirus E2 protein, the method comprising:

providing a first set of nuclear magnetic resonance chemical shifts for atoms of a mixture comprising the ligand and the HPV-18 strain of papillomavirus E2 protein; wherein the chemical shifts are assigned to atoms of the protein;

causing the first set of chemical shifts to be entered into memory of a computer;

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causing the computer to read a second set of chemical shifts as listed in Table 1 from a machine-readable data storage medium;

causing the computer to compare the first and second sets of chemical shifts; and

causing the computer to identify at least a portion of the atoms that exhibit changes in chemical shifts, wherein the ligand binding site comprises the identified atoms.

18. (Cancelled)

19. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one proton that either exhibits a change in ¹H chemical shift of at least about 0.04 ppm or is no longer observed.

20. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify at least one carbon atom that either exhibits a change in ¹³C chemical shift of at least about 0.2 ppm or is no longer observed.

21. (Original) The method of claim 17 wherein causing the computer to identify at least a portion of the atoms comprises causing the computer to identify a nitrogen atom that either exhibits a change in ¹⁵N chemical shift of at least about 0.2 ppm or is no longer observed.

22. (Original) The method of claim 17 further comprising causing the computer to visually display a spatial arrangement of atoms of the ligand binding site.